U.S. Nuclear Regulatory Commission (NRC)
Advisory Committee on the Medical Uses of Isotopes (ACMUI)

Revision 2 to Regulatory Guide 8.39, "Release of Patients Administered Radioactive Materials"

Final Report
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Charge

During the September 20-21, 2018, ACMUI Meeting, ACMUI Chairman, Dr. Christopher Palestro, established a subcommittee to review the NRC staff's draft proposed revisions to Regulatory Guide (RG) 8.39, "Release of Patients Administered Radioactive Materials."

Background

The NRC's RG 8.39, Revision 0, was issued in April 1997, following the rule change in 10 CFR 35.75 to allow the release of patients administered radioactive material on a solely dose-based criteria. Since that time, there have been several challenges to the appropriateness of the release criteria and the associated precautions that are required to be provided to minimize radiation exposure to other individuals from the released patient. Over the past several years, the NRC staff has conducted an extensive evaluation, which included a review of published literature, and stakeholder engagement with licensees, patients, and Agreement States, to determine whether significant regulatory changes to the patient release program are warranted. A summary of this evaluation can be found in SECY-18-0015 "Staff Evaluation of the U.S. Nuclear Regulatory Commission's Program Regulation Patient Release After Radioisotope Therapy".[1] One of the recommendations was that the guidance in RG 8.39 should be updated, simplified, and made clearer and more explicit.

The revision of RG 8.39 is being conducted in two phases. Phase 1 revision of RG 8.39, which was completed in April 2020, updated the patient release guidance, including information for patient instructions and updates to Table 3, "Activities of Radiopharmaceuticals that Require Instructions and Records When Administered to Patients who are Breast-Feeding an Infant or Child." This ACMUI subcommittee's review and recommendations for Phase 1 can be found in our previous subcommittee reports.[2,3] The following Subcommittee comments and recommendations pertain to the Draft Phase 2 revision to RG 8.39, which updates the dosimetric equations, methodologies, and tables used to calculate dose to members of the public from released patients.

General Comment:

The Subcommittee commends the NRC for their efforts in updating the guidance to licensees on meeting the patient release criteria. The Subcommittee also acknowledges and appreciates that most of the recommendations from its two previous reports on the Phase 1 Revision of RG 8.39 have been incorporated. However, the draft Phase 2 Revision has made changes to the patient instructions, therefore, this content area will be included again in our comments and recommendations. The subcommittee recognizes that while this guidance document is primarily intended for licensees, it will also be viewed by patients, and their family and friends, so it is important for the content to be clear and easy to understand.

Summary of Recommendations

1. In the Content of Instructions Section (4.2), the subsections should be reordered to the original sequence: (1) Pretreatment Discussions on the Administration of Radiopharmaceuticals, (2) Patient Precautions, (3) Patient Instructions, (4) Patient Acknowledgement of Instructions. It is important to emphasize upfront that the major source of radiation dose to other individuals will be from external exposure from the patient. Therefore, the most important precautions to take are measures to reduce or avoid the external radiation exposure from the patient, especially in the early time period after administration of the radionuclide therapy. This is discussed in the Patient Precautions subsection and so it should precede the Patient Instruction subsection. While the release instructions may also include measures to limit the transfer of radioactive contamination to others, they should not overshadow or distract from the external precautions, nor should it cause patient anxiety, as the radiation doses from internal exposure have been demonstrated to be small or negligible.[4, 5] Suggested rewording of the patient instructions to make them more clear and easy to understand, and elimination of some precautions that have little effect in reducing bystander dose has been provided in the specific comments.

2. The basic administered activity thresholds in Table 1, and corresponding measured dose rates in Table 2, for the release of patients (and for providing instruction) were calculated assuming an occupancy factor of 100% at 1 meter. An occupancy factor of 1.0 is unrealistic and cannot be justified for routine application, even for radionuclides with a physical half-life less than one day. The corresponding activity and dose rate values are extremely conservative, and a factor of four lower than what is currently in RG 8.39 Revision 1. This will result in an increased need for licensees to perform patient specific dose calculations and provide patient instructions at activity levels much lower than previously required. This guidance is also not consistent with the record keeping requirement in 10 CFR 35.2075(a), which only requires a record of the release if using an occupancy factor less than 0.25 at 1 meter. It is recommended that the activity and dose rate values in Tables 1 and 2 be calculated with an occupancy factor of 0.25 at 1 meter, to be more realistic and compatible with 10 CFR 35.2075(a).

3. Sections 1.3 and 3.3 “Release of a Patient After a Hold Time” require the licensee to calculate the amount of time the patient release must be delayed for either radioactive decay or biological elimination to reduce the administered activity down to the threshold value in Table 1. Holding a patient after administration of a radiopharmaceutical to allow for some level of decay or biological elimination is not a current practice in the United States. Licensees will either use an effective half-life for a patient specific dose calculation or the measured exposure rate for release of the patient. This section should be removed as it is not

a practical option due to the length of holding time typicaly required to reduce the retained activity.

4. The Patient-Specific Modifying Factors and Methods presented in Appendix B, and Example Calcultions illustrated in Appendix C, are overly complex and require an unrealistic level of knowledge of extended patient behavior following release. While this calculational methodology is an admirable academic exercise, it is not practical for licensees to use for authorizing and documenting patient release using patient specific factors. Determining "Time Durations" for Travel, Instruction, and Afterward in units of effective half-lives, and the corresponding fraction of time a bystander spends in close contact with the patient during these periods would be unworkable. While the Geometric Modifying Factor accounts for varying bystander separation distances and source-receptor configurations, it again requires an unrealistic detailed knowledge of patient and bystander behavior following release. The Attenuation Modifying Factor tables account for photon scatter, buildup, and absorption at different patient tissue thicknesses, however, buildup is not applicable for distributed sources within the body and accurately determining the overlying tissue thickness would be much more challenging than simply measuring the dose rate from the patient after administration of the radiopharmaceutical. To be of practical operational value, the model needs to be simplified, such as that in the current RG 8.39 or the RADAR Patient Exposure Radiation Dose Calculator.[6] Consideration should be given to eliminating the geometric and attenuation modifying factors, keeping the biokinetic modifying factor (effective half-life) and simplifying the occcupancy modifying factor to single values of 0.5, 0.33, 0.25, 0.125, and 0.0625 for various patient/bystander conditions or situations. Examples of the possible occupancy conditions could be:
    a. Patient is unable or unwilling to follow any instructions (0.5)
    b. Patient requires significant medical care or living assistance (0.33)
    c. Patient will be around other members of the household and public but will follow instructions (0.25)
    d. Patient lives alone but will have potential contact with members of the public and will follow instructions (0.125)
    e. Patient lives alone and will not have any contact with others and will follow instructions (0.0625)

   Attachment 1 contains a sample patient questionnaire that could be used to ascertain the information to assign the appropriate occupancy factor.

5. In Section 6 "Material Separated from the Patient", it states that the dose limits in 10 CFR Part 20 apply to exposure from radioactive material separated from a released patient. The Subcommittee strongly disagrees with this position. Since the dose limits in 10 CFR Part 20 do not apply to radiation exposure from a patient released in accordance with 10 CFR 35.75, it is only reasonable that this would also apply to exposure from any radioactive material that the patient excretes or physically separates from the patient, with the exception of temporary implants. A licensee cannot practically control or predict, nor would they be able to know or evaluate if an event occured where radioactive material separated from a patient caused an exposure to a bystander. It is illogical and impractical for radioactive material that separates from a patient released in accordance with 10 CFR 35.75 to become "licensable" again under the licensee that administered it to the patient (with the exception of temporary implants which are still covered under the license even though the patient has been released).

6. In Section 4.3 "Death of a Patient Following Radiopharmaceutical Administration or Implants," the results of an analysis indicate that for several radionuclides, dose rates exceeding 0.02 mSv/h or total doses in excess of 1 mSv are possible if unexpected death were to occur within days of release and knowledge of the radioactive administration is not communicated. It should be noted that the analysis made very conservative assumptions. The dose rate was calculated only 6 hours after administration with no acccount for biological elimination, and the total dose was calculated for an exposure from hour 12 to 32 at a distance of 1 meter with full occupancy and no account for biological elimination. Therefore, the likelihood of these dose rates and integrated doses occurring from a decedent previously administered radionuclide therapy is exceedingly small. It would be helpful if a similar type of analysis were performed of the potential exposures from cremation of a body containing radioactive material, specifically, exposure to crematorium staff and exposure to the public from effluent releases.

Specific Comments:

Pg 1, Purpose: Continue the sentence "This RG also provides licensees with a methodology to modify the threshold …." in the first paragraph and start a new paragraph with the sentence "In addition, the RG provides licensees with instructions for patients…".

Pg 2, Applicable Regulations, 10 CFR 35.75(b): Change last sentence to read "If the dose to a breastfeeding infant or child could exceed an effective dose equivalent of 1 mSv (0.1 rem) without the patient's interruption of breastfeeding, written instructions must be given to the nursing mother on (1) guidance on the interruption or discontinuation of breastfeeding and (2) information on the potential adverse consequences if breastfeeding is not ceased or discontinued.

Pg 3, Table of Contents: Delete Section 3.3 Release of Patients After a Hold Time.

Pg 3, Table of Contents: 4.2 Content of Instructions, Reorder sequence of subsections to: (1) Pretreatment Discussions on the Administration of Radiopharmaceuticals, (2) Patient Precautions, (3) Patient Instructions, (4) Patient Acknowledgement of Instructions.

Pg 4, Background: In first sentence change 1979 to 1997.

Pg 5, Consideration of International Standards: Second paragraph, change (rem) to (tenths of rem).

Pg 7, Section 1 release Criteria: Consider using the exposure rate constant readily available in the literature[5,6] for Δ_{pr} instead of a calculated dose rate constant. It will be much simpler to obtain for new radionuclides and it does not differ significantly from the calculated dose rate constant.

Pg 8, Section 1, fourth paragraph: Delete the last sentence, "In addition, licensees may need to consider both internal and external exposure to a bystander from byproduct material which could have become separated or excreted from a patient…". It is impractical for a licensee to control or predict the exposure to a bystander from radioactive material separated (excreted) from a patient.

Pg 9, Table 1: The activity threshold for C-14 is unrealistically low due to its extremely long half-life and theoretical exposure from a patient.

Pgs 9, 11, and 14: Add Ac-225 to Tables 1, 2, and 3.

Pg 11, Table 2: The measurement thresholds for C-14, Ru-106, and Sr-90 are less than background levels (approximately 0.02 mR/hr) and cannot be accurately measured. A footnote should be added to state "Activity and dose rate limits do not apply to these radionuclides because of the minimal exposures to members of the public resulting from dosages normally administered for diagnostic or therapeutic purposes." Also, listing PET isotope measurement thresholds over 1 R/hr is imprudent.

Pg 12, Section 1.3 Release of a Patient After a Hold Time: This section should be deleted as it is not a practicle option due to the length of holding time for physical decay. Licensees will either use an effective half-life for a patient specific dose calculationor or the measured exposure rate for release of the patient.

Pg 13, Section 2 Breastfeeding Patients: First paragraph, 1st sentence, add the word "written" before "instructions and change the word "were" to "was". Second paragraph, 3rd sentence, Change the word "were" to "was".

Pg 14, Section 2, Table 3: Values in Column 1 and Column 2 that are less than 1 microcurie (or some similarly low value) should just be noted as record/instructions required. Listing nanocurie or lower values is not helpful with respect to medical use quantities.

Pg 15, Section 2, Table 4: For the very long recommended interruption times, it would be better for the guidance to say, "complete cessation for this child". Having a specific number 1400 hours vs. 1700 hours etc. is not practical for patients to follow. No nursing mother should be led to think that a 1400-hour interruption should be considered.

Pg 16, Section 3 Patient Specific Dose Calculations: First paragraph, in the sentence "In the basis, licensees must document any patient-specific modifying factors used in the calculation and a general description of how that information was acquired…", Change the word "must" to "should" as there is no regulatory requirement to document how patient specific information was obtained.

Pg 16, Section 3 Patient Specific Dose Calculations: First paragraph, Delete the sentence "Patient instructions must match or be more limiting than patient-specific factors used to release patients…" as there is no requirement to match patient instructions to patient specific dose calculations.

Pg 17, Section 3.1 Release of Patients Based on the Administered Activity: First sentence, "licensees may calculate patient-specific thresholds on a case-by-case basis." There should be an option to create a class or category of general patient specific factors applicable to multiple patients.

Pg 17, Section 3.1 Release of Patients Based on the Administered Activity: Second paragraph, delete "or based on a calculated hold time in Section 3.3".

Pg 17, Section 3.2 Release of Patients Based on the Measured Dose Rate: Delete "c. Calculate a hold time described in Section 3.3".

Pg 17, Section 3.3 Release of a Patient After a Hold Time: Delete section as it is not practical to hold a patient to allow for decay or biological elimination in order to allow for release.

Pg 20, Second paragraph: Delete the sentence "I-131 is currently the medical radioisotope of highest concern, as it is the most commonly used radionuclide in radiopharmaceutical therapy…"

as it will soon be surpassed by other radiopharmaceuticals and volatility is not an issue with I-131 inside a patient's body.

Pg 20, Second paragraph: Change second sentence to read "The regulations in 10 CFR 35.75 apply to all medical radioisotope therapies such as iodine (I)-131, yttrium (Y)-90, I-125, cesium (Cs)-131, lutetium (Lu)-177, radium (Ra)-223, and actinium (Ac)-225.

Pg 21, Under (3): Change second sentence to read "Patients who travel via motor vehicle, boat, or airplane through international border checkpoints are subject to screening for radiation.

Pg 21, Section 4.2.4 Patient Precautions should follow Section 4.2.1 Pretreatment Discussions on the Administration of Radiopharmaceuticals to place the emphasis on external exposures and precautions.

Pg 22, Third paragraph: Delete the sentences "To ensure dose limits are not likely to be exceeded, licensees must ensure patients can follow instructions if they are used to justify patient-specific modifying factors to demonstrate exposures will be less than 5 mSv (0.5 rem). Pre-treatment discussions with patients, or caregivers, such as those described in the section above, can help a licensee determine if a patient is able to follow the instructions and identify patients who cannot. If a patient is unable or unwilling to follow necessary instructions for release, they may need to be held longer than others with similar administrations." as it is redundant with what is stated in the previous paragraph.

Pg 22, Patient Instructions a-l: Suggest replacing the patient instructions a-l with the following to be more clear, concise, and consistent with the Patient Precaution section:

1. Minimize the time you spend in close contact with other individuals, especially pregnant women and young children (a general guideline is no closer than 3 feet for more than 1 hour per day). Try to maximize your distance from others as much as possible (6 feet).

2. Avoid direct contact or sharing of personal items which may result in the contamination of others with your body fluids (saliva, urine, sweat), especially pregnant women and young children.

3. Sleep alone in a separate bedroom. Avoid kissing or any intimate contact with another person.

4. If possible, have sole use of a bathroom (males should sit to urinate to avoid splashing).

5. Use good hygiene habits, wash your hands frequently. Use separate towels and washcloths.

6. Avoid handling or preparing food for others. Use separate dishes, cups, and eating utensils.

7. Avoid public facilities and the use of public transportation if possible.

8. Maintain good hydration, as directed by a physician.

9. If you need any medical care, the medical personnel should be informed about these instructions.

10. You should be aware that radiation detection devices used at border crossings, airports and federal facilities for homeland security purposes may be sensitive enough to detect the radioactivity levels in your body for up to several weeks. You should carry these instructions when you travel and provide them to law enforcement authorities if detained for triggering a radiation monitor.

Pg 23, First paragraph: Delete the sentence "The licensee should also inform the patient on how to clean up an area contaminated with body fluids (e.g., urine, vomit) and how to dispose of the cleaning materials." As it has been previously stated multiple times and the emphasis should be on external exposures.

Pg 23, Section 4.2.4 Patient Precautions, a. (1): Change first sentence to read "Emphasize the importance of keeping an adequate distance from others, especially children and pregnant women and to also minimize the time near others." Delete the sentences "Can arrangements be made for family members (including children and any pregnant household members) to lodge elsewhere temporarily? Or can another individual come and take care of the children and any pregnant household member in their home." The emphasis is simply to maintain an adequate distance from others, especially children and pregnant women.

Pg 24, Section 4.2.4 Patient Precautions, a. (3): Change sentence to read "Emphasize for the patient to sleep separately and abstain from all forms of intimate contact."

Pg 24, Section 4.2.4 Patient Precautions, b. (1): Change sentence to read "Encourage the patient not to prepare or share food with others and to use separate dishware and eating utensils."

Pg 24, Section 4.2.4 Patient Precautions, b.: Delete items (3), (4), and (5) as they are excessive, arbitrary, and not likely to reduce exposure to others.

Pg 25: Delete first full paragraph "The licensee may encourage patients to have available plastic bags, disposable gloves and wipes before treatment…." as this is redundant with the previous statement in this section.

Pg 25, Section 4.3 Death of a Patient Following Radiopharmaceutical Administration or Implants: It should be noted that the analysis made very conservative assumptions. The dose rate was calculated only 6 hours after administration with no acccount for biological elimination, and the total dose was calculated for an exposure from hour 12 to 32 at a distance of 1 meter with full occupancy and no account for biological elimination.

Pg 26, Section 4.3 Death of a Patient Following Radiopharmaceutical Administration or Implants: Change last sentence to read "The administering licensee should provide precautions to the funeral director for family members and the public to follow during visitation prior to burial or internment."

Pg 26, Records of Release: First paragraph, last sentence: Delete "or greater than 1" as this is unrealistic for exposures from a patient.

Pg 26, Records of Release: Delete "c. For Delayed Release of a Patient Based on a Radioactive Decay Calculation" as this is not used.

Pg 27, Section 6 Material Separated from the Patient: The dose limits in 10 CFR Part 20 do not apply to radiation exposure from a patient released in accordance with 10 CFR 35.75. This would also apply to exposure from any radioactive material that the patient excretes or physically separates from the patient, with the exception of temporary implants. A licensee cannot practically control or predict, nor would they be able to know or evaluate, if an event occured where radioactice material separated from a patient caused an exposure to a bystander. It is illogical and impractical for radioactive material that separates from a patient who has been released in accordance with 10 CFR 35.75 to become "licensable" again under the licensee that administered it to the patient (with the exception of temporay implants whcih are still covered under the license even though the patient has been released).

References

1. NRC Policy Issue (Information) SECY-18-0015, "Staff Evaluation of the U.S. Nuclear Regulatory Commission's Program Regulation Patient Release After Radioisotope Therapy", January 29, 2018
2. ACMUI, Subcommittee Review and Comments on Draft Proposed Regulatory Guide 8.39, "Release of Patients Administered Radioactive Materials," Revision 1 (Phase 1) Final Report, June 19, 2019
3. ACMUI, Subcommittee Review and Comments on Final Draft Proposed Regulatory Guide 8.39, "Release of Patients Administered Radioactive Materials," Revision 1 (Phase 1) Final Report, March 25, 2020
4. NRC Publication, "Patient Release After Radionuclide Therapy – A review of the Technical Literature, Dose Calculations, and Recommendations", Reviewed by Shaheen Dewji and Nolan Hertel, September 25, 2017
5. RCD Radiation Protection Associates. "Activity Thresholds, Patient-Specific Modifying Factors, Breastfeeding Interruption Times, and Other Supporting Data," Research Information Letter Report for Phase 2 Revisions to Regulatory Guide 8.39: Release of Patients Administered Radioactive Material. RCD-21-181-0. Corvallis, OR. June 30, 2021. (ML21214A223)
6. RADAR Exposure and Dose Calculator (doseinfo-radar.com)
7. International Commission on Radiological Protection (ICRP). Nuclear Decay Data for Dosimetric Calculations. Annals of the ICRP. Publication 107. 38(3). 2008.
8. Smith, DS, Stabin MG, "Exposure Rate Constants and Lead Shielding Values for Over 1,100 Radionuclides", Health Physics (102(3):271-291), 2012

Respectfully submitted,

Subcommittee on Regulatory Guide 8.39 Release of Patients Administered Radioactive Materials,
Advisory Committee on the Medical Uses of Isotopes
U.S. Nuclear Regulatory Commission

The ACMUI unanimously approved this report as presented during its public teleconference meeting on December 15, 2021.

Attachment 1

PATIENT QUESTIONNAIRE FORTREATMENT WITH IODINE – 131

Patient Name: _____ Referring Physician: _____

MRN: _____ Patient Age: _____

1. **Confirmation that the patient is not pregnant (12-55 yrs.)**
   Date of negative pregnancy test: _____ (Must be within 24 hours of dosing)
   Other (Age, Tubal Ligation, or Hysterectomy): _____

2. **Is the patient breastfeeding? Yes _____ No _____**

3. **Where will the patient reside after administration of the therapeutic dose?**
   _____

4. **How will the patient travel to place of residence and who will be traveling with the patient?**

   _____

5. **List the age and relationship of all other household members who will be staying with the patient when they get dosed?**
   _____

   _____

6. **Will there be any young children (<10 yrs) or pregnant women at home when the patient returns after treatment? Yes _____ No _____**

7. **Will the patient be responsible for the primary care of any young children or individuals requiring living or medical assistance? Yes _____ No _____**

8. **Is the patient scheduled for travel or vacation for 2 wks after dosing?**
   Yes _____ No _____

9. **What is the patient's occupation and specific job duties?**
   _____

   _____

10. **Can the patient remain home from work for the recommended time?**
    Yes ___ No ___ NA ___

11. **Does the patient require any special medical care or living assistance? Yes ____ No _____**

12. **Is the patient incontinent or have any urinary bladder control problems? Yes ____ No____**

13. **Are there any other issues that would prevent the patient from being able to comply with radiation safety instructions? Yes _____ No _____**

    Explain: _____

Individual completing questionnaire: _____ Date: _____

Prescribed Dose:_____% Uptake: _____